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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/068,133	02/05/2002	Howard Kaufman	MDS-013AC2	8486
51414	7590	03/10/2006	EXAMINER	
GOODWIN PROCTER LLP PATENT ADMINISTRATOR EXCHANGE PLACE BOSTON, MA 02109-2881			MOSS, KERI A	
			ART UNIT	PAPER NUMBER
			1743	

DATE MAILED: 03/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/068,133

Applicant(s)

KAUFMAN ET AL.

Examiner

Keri A. Moss

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 33-60 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 33-60 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☒ Claim(s) 34-39, 46, 47, 49 and 50 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 2/5/02 and 6/2/02 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 2/5/02; 5/24/02; 1/12/04; 1/23/05
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____

DETAILED ACTION

Election/Restrictions

1. This application contains claims directed to the following patentably distinct species: claims 34 and 35, locally applying step. The species are independent or distinct because they involve mutually exclusive procedures, one a topical procedure, the other an invasive procedure. The second species are claims 36-39, the processing step. They are distinct because each addresses different problems in data collection. The third species are claims 46 and 47, the type of sample. They are distinct because the samples are tissues from two different organ systems. The fourth species are claims 49 and 50, the chemical agent. They are distinct because they claim mutually exclusive chemicals.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 33 and 48 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after

the election, applicant must indicate which are readable upon the elected species.

MPEP § 809.02(a).

1. During a telephone conversation with Dr. William Haulbrook on February 24, 2006 a provisional election was made with traverse to prosecute the invention of topically applying chemical agent, claim 34. Applicant in replying to this Office action must make affirmation of this election. Claims 35, 36, 37, 39, 50 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

2. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Drawings

3. The drawings are objected to under 37 CFR 1.83(a). The drawings must show every feature of the invention specified in the claims. Therefore, the compensation map and alignment of the feature present must be shown or the feature(s) canceled from the claim(s). No new matter should be entered.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure

number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 33-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 20, the terms "correlating" and "correlate" are unclear. How are the images correlated? Are mathematical comparisons made between the images? If so, what is the calculation? Upon what is the correlation based? What is being compared? Please provide a definition.
6. Claims 33-60 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the

steps. See MPEP § 2172.01. The omitted steps are: how the images are correlated.

Are mathematical calculations done? What is being compared in the correlation?

Examiner interprets correlate to mean to note the linear relationship between two variables.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 33-34,38,40-45,48-49,51-56, 58 and 60 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Tadrous, Paul, "Methods for imaging the structure and function of living tissues and cells: 2. Fluorescence lifetime imaging," J Pathol 2000; 191: 229-234. Tadrous discloses locally applying a chemical agent to a sample (Introduction); obtaining a plurality of sequential images of said sample (p.231 1st paragraph); and processing at least two sequential images to correlate at least two sequential images (p.231 1st and 2nd paragraph). While Tadrous's method does not involve addition of a chemical agent, Tadrous indirectly discloses applying a chemical agent by implying that using stain is

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the general procedure (Introduction). The correlation step is disclosed because the bound:unbound fura-2 ratio is determined over time. The chemical agent, stain, is inherently applied topically. The processing step may comprise compensating for relative motion between the sample and a detection device (p.230 paragraph bridging columns). The processing step comprises constructing a compensation map (Figure 2) based on a change in position of a feature (GFP-cyclin-B1) present in the sequential images and aligning this feature. The plurality of sequential images comprises measurements of a fluorescence spectrum produced by an endogenous chromophore (see e.g., fura-2 p.231 paragraphs 1-3). The endogenous chromophore may also be NADH, elastins, or collages (p.231 paragraphs 5-6). The chemical agent, stain, inherently interacts with the sample to alter an optical signal produced by the sample.

The processing step may comprise constructing a compensation map based in part on a change in position of a feature in each of at least two sequential images and aligning the feature present using the compensation map (p.233 1st paragraph). The image compensation information is used to process an optical signal, fluorescent light, from the sample. The images are used to determine morphological characteristics of the sample, such as size or shape. This determination is based on a change in an optical signal from said area of the sample (p.233 1st paragraph). The article of manufacture that carries out the above method has computer-readable program means with computer-readable instructions (p.233 2nd paragraph).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 46 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tadrous, supra. Tadrous does not expressly disclose a sample comprising human

cervical tissue or determining the abnormal health of the tissue. However, Tadrous does disclose a sample of human breast tissue and further teaches that the disclosed method identifies abnormal health in breast tissue (p.231 right hand column 2nd full paragraph). Tadrous teaches that because its imaging modalities may provide the best ever chance of getting a truly useful marker of benign versus malignant cells and tissues, more studies must be followed up and expanded. Tadrous thereby encouraged further experimentation with the disclosed imaging techniques. It would have been obvious to one of ordinary skill in the art to experiment with the Tadrous imaging technology on different tissues. Therefore it would have been obvious for one to try several different types of human tissues, including cervical tissue, to test whether Tadrous imaging distinguishes between malignant and benign cells for such tissues.

13. Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tadrous in view of Richards-Kortum (USP 6,241,662). Tadrous does not disclose using a chemical agent selected from a group consisting of acetic acid, formic acid, propionic acid and butyric acid. Richards-Kortum teaches using acetic acid to enhance the optical return signal of illuminated tissue during fluorescence microscopy, specifically for epithelial tissue such as cervical (column 2 lines 43-65). An additional advantage to using acetic acid is that when used in fluorescence microscopy it enables diagnosis of the tissue as normal or abnormal (column 6 lines 15-27). Therefore it would have been obvious to one of ordinary skill in the art to use acetic acid as a chemical agent for

enhancing the optical signal in fluorescence microscopy and to gain the additional advantage of detecting abnormal cells.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 33, 38 and 46 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 27, 28 and 31 of copending Application No. 09/738147. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 33, 38 and 46 are the genus of species claims 27, 28 and 31 of Application No. 09/738,147. Claim 27 discloses a narrower type of processing step as aligning the plurality of images. The species claims 27, 28 and 31 anticipate the genus claims 33, 38 and 46.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

16. Claim 33 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 56 of copending Application No. 10/828624. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 33 is the genus of claim 56 of Application No. 10/828624 because claim 56 specifies the type of image obtained as a fluorescence signal. The species claim 56 anticipates the genus claim 33.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

17. Claims 33, 38 and 46 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 27, 28 and 31 of copending Application No. 10/411,777. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 33, 38 and 46 are the genus of claim 27, 28 and 31 of Application No. 10/411,777 because claim 27 specifies the type of processing step as aligning the plurality of images. The species claims 27, 28 and 31 anticipate the genus claims 33, 38 and 46.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

18. Claims 33, 41-43, 46 and 49 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 8, and 10 of U.S. Patent No. 6,933,154 (hereinafter '154). Although the conflicting claims are not identical, they are not patentably distinct from each other because '154 claims 1-4, 8 and 10 are a species of instant genus claims 33, 41-43, 46 and 49. '154 Claim 1 has narrower limitations of the instant application claims, including teaching 1) applying the chemical agent acetic acid, 2) obtaining at least one optical signal as the image obtaining step (note here that "at least one" reads on "a plurality") and 3) identifying a characteristic of the region as the processing step. The species '154 claims 1-4, 8 and 10 anticipate the genus of instant application claims 33, 41-43, 46 and 49.

Conclusion

19. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Chien-Chuan Ko et al, "Multiresolution registration of coronary artery image sequences," International Journal of Medical Informatics 44 (1997) 93-104 teaches a formula for registering changes between two images.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Keri A. Moss whose telephone number is 571-272-8267. The examiner can normally be reached on 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571)272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

KAM 3/6/06



**LYLE A. ALEXANDER
PRIMARY EXAMINER**